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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,455	VAN DER BURG ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE T. HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *13-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-12* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on *05/18/2009* in response to office action mailed on 03/27/2009 has been acknowledged.

Claims 1-12 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Restriction of invention

Applicant's election with traverse of restriction requirement in the reply filed on May 18, 2009 is acknowledged. Applicant elects with traverse the invention Group I (Claims 1-12) for further prosecution on merits. Because the applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Therefore restriction as indicated is proper and made final.

Claims 1-12 are pending and presently under examination.

Claims 13-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected claims, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph.

Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for lack of conclusion. How is the “determining” step (step “d”) indicative of the presence or

absence of one or more specific ligands as recited in the preamble. Hence the artisan would not know if the claim is complete.

Claim 1 rejected under 35 U.S.C. 112, second paragraph for the absence of specific direction of the performance of the “determining” step (step “d”). The recitation "based on said comparison" in (step ‘d’ is vague, and does not indicate that the presence of a ligand is determined by the reporter that is expressed (i.e., the determining should be indicated by an increased or change in activity).

Regarding claim 4, the phrase "preferably" renders the claim indefinite because it is not known if the preferable three cell lines is required of the claimed invention. See MPEP § 2173.05(d).

Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses ligands for any and/or a ll specific components of pathway and wherein specific component is a ligand modifying factor thus broadly embracing all cellular components involved in a ligand binding and all enzymes or factors involved in the modifying ligand expression and those involved in post translational modifications etc., such as phosphorylation, glycosylation, methylation, sulfonylation, etc., thus encompassing huge number of genuses and species of the super genuses of ligands and their modifiers..

At the best he specification only teaches steroid ligand receptor ligands and ane the enzymes involved in metabolic conversion into different steroids (converting enzymes; Fig.3) as the only modifiers of said steroid ligands.

The application does not disclose any othe specific cellular ligands or the ligand modifiers of said broadly claimed specific components.. Thus the number of examples provided does not commensurate with the scope and breadth of instant claims.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics .

Since the specification fails to disclose other claimed ligands or ligand modifying factors other than that of steroid lignds in cells, it is not possible to envision the broadly claimed ligands and ligand modifiers. Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention..

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the

treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 and 4-5, are rejected under 102(e) as being anticipated by Stuelpnagel et al., (US2005/0158702 A1).

The above claims are drawn to a method for determining the presence of one or more specific ligands in a sample comprising steps of contacting the sample with an array of cell lines comprising a reporter gene construct respnding a cellular pathway induced by different specific ligands, measuring the activity of reporter gene and determining by comparison the ligands in the sample.

Regarding claims 1-2 and 4-5 Stuelpnagel teaches a biosensor array of one or more cells or cell lines and relies on the fact that individual cells which are biologically or chemically stimulated by the ligands in the cell environment and respond by producing a change in the cell or cellular environment wherein said cell may comprise genetically engineered cells that are prokaryotic or eukaryotic, mammalian, primate etc and cell lines of any type for example osteoblast cells or chondrocytes etc (entire article; abstract; paragraphs 0030, 033-036, 0057-058). In general the cells are transformed using variety of vectors and constructs and used for functional assay of various analytes including biomolecules such as steroids etc (paragraphs 0096-0099) and in one embodiment the cell plasmids regulates the expression of marker or reporter genes such as luciferase or encoded GFPs (paragraphs 0111-0113) depending on the ligands or their concentrations in the sample. Thus the rejected claims are within the scope of the Stuelpnagel's disclosure.

Claims 1-2 and 4-5, are rejected under 102(b) as being anticipated by Walt et al., (US 6210910B1).

The above claims are drawn to a method for determining the presence of one or more specific ligands in a sample comprising steps of contacting the sample with an array of cell lines comprising a reporter gene construct respnding a cellular pathway induced by different specific ligands, measuring the activity of reporter gene and determining by comparison the ligands in the sample.

Regarding claims 1-2 and 4-5 Walt teaches a biosensor array of individual cells or randomly mixed population of cells having unique response characterstic to or chemical or biological materials or target analytes in the cell environment and respond by producing a change in the cell or cellular environment in a detectable manner (entire article; abstract; col.5, lines 55-68 briding col.6-9). Said cells of biosensor may comprise genetically engineered cells that are prokaryotic or eukaryotic, mammalian, primate etc and cell lines of any type for example osteoblast cells or chondrocytes etc (entire article; col.9, lines 35-54). In an embodiment the cells are transformed using variety of vectors and constructs and used for functional assay of various analytes including biomolecules such as steroids etc (co.l27) and regulate the expression of marker or reporter genes such as luciferase or encoded GFPs (col.15, lines 15-42; col.28) depending on the ligands or their concentrations in the sample. Thus the rejected claims are within the scope of the Walt's disclosure.

Claims 1-2, 4-5 and 11-12 are rejected under 102(e) as being anticipated by Giuliano et al., (US 2003/0096322 A1).

The above claims are drawn to a method for determining the presence of one or more specific ligands in a sample comprising steps of contacting the sample with an array of cell lines comprising a reporter gene construct respnding a cellular pathway induced by different specific ligands, measuring the activity of reporter gene and determining by comparison the ligands in the sample.

Regarding claims 1-2, 4-5 and 11-12 Giuliano teaches a biosensor array of one or more cells or cell lines for optical analysis of to rapidly determine the compounds in the environment that particularly affect particular biological functions of cells such as protease mediated translocation and apoptosis, kinase activity, transcription factor activity and in an embodiment the invention provides recombinant nucleic acids encoding a protease biosensor (entire article; Abstract; paragraphs 033-044; Fig.32; 0555-058). Giuliano teaches cell arrays wherein said cell may comprise genetically engineered cells that are of any type (entire article; abstract; paragraphs 033-035, 0074-0080). Thus the rejected claims are within the scope of the Giuliano's disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-8 are rejected under 35 USC 103 (a) as being unpatentable over Stuelpnagel et al., (US2005/0158702 A1).applied to claims 1-2 and 4-5 as above and in view of Wilson et al et al (2002, Toxicological Sciences 66:69-81; art of record).

The above claims are drawn to a method for determining the presence of one or more specific ligands in a sample comprising steps of contacting the sample with an array of cell lines comprising a reporter gene construct respnding a cellular pathway induced by different specific ligands, measuring the activity of reporter gene and determining by comparison the ligands in the sample.

Regarding claims 1-2 and 4-5 Stuelpnagel teaches a biosensor array of one or more cells or cell lines and relies on the fact that individual cells which are biologically or chemically stimulated by the ligands in the cell environment and respond by producing a change in the cell or cellular environment wherein said cell may comprise genetically engineered cells that are prokaryotic or eukaryotic, mammalian, primate etc and cell lines of any type for example osteoblast cells or chondrocytes etc (entire article; abstract; paragraphs 0030, 033-036, 0057-058). In general the cells are transformed using variety of vectors and constructs and used for functional assay of various analytes including biomolecules such as steroids etc (paragraphs 0096-0099) and in one embodiment the cell plasmids regulates the expression of marker or reporter genes such as luciferase or encoded GFPs (paragraphs 0111-0113) depending on the ligands or their concentrations in the sample. Stuelpnagel et al however, does not teach specific component of a steroid hormone receptor or thyroid hormone receptor.

Wilson teaches the limitation of plasmids expressing specific hormone receptors and deriving a cell line that could be used as an effective cell based biosensor for detecting several steroid hormones and for screening androgen agonists and antagonists

etc. wherein cells could be arrayed in 96 well plates and effectively used for screening hormonally active chemicals (entire article; abstract).

Thus it would have been obvious for one of ordinary skill in the art to substitute generic biosensor cells in Stuelpnagel live cell based biosensor arrays with the biosensor cells equipped with reporter gene expression vectors for effectively detecting steroid hormones and related chemical in the cellular environment as taught by Wilson and use said cell array for detecting ligands that affect pathways related to steroid receptors. One of ordinary skill in the art would have bee motivated to make and use cell arrays with hormone and related compound detection ability as taught above as they are effective in detecting environmental contaminants of hormonally active ligands/chemicals that could effect human and animal health. One of ordinary skill in the art would have reasonable expectation of success making and using biosensor cell arrays because the art teaches that it is routine to make a biosensor arrays of live cells expressing reporter genes for detecting chemicals affecting any particular cell pathways and the art further teaches that it is routine to make biosensor cells for detecting specific steroid hormones and related chemicals/ligands in the environment. Thus, the claimed invention was *prima facie* obvious.

Claims 3, 6-8 & 10 are rejected under 35 USC 103 (a) as being unpatentable over Stuelpnagel et al., (US2005/0158702 A1).applied to claims 1-2 and 4-5 as above and in view of Quaedackers et al et al (2001, Endocrinology 142:1156-1166; art of record).

The above claims are drawn to a method for determining the presence of one or more specific ligands in a sample comprising steps of contacting the sample with an array of cell lines comprising a reporter gene construct respnding a cellular pathway induced by different specific ligands, measuring the activity of reporter gene and determining by comparison the ligands in the sample.

Regarding claims 1-2 and 4-5 Stuelpnagel teaches a biosensor array of one or more cells or cell lines and relies on the fact that individual cells which are biologically or chemically stimulated by the ligands in the cell environment and respond by producing a

change in the cell or cellular environment wherein said cell may comprise genetically engineered cells that are prokaryotic or eukaryotic, mammalian, primate etc and cell lines of any type for example osteoblast cells or chondrocytes etc (entire article; abstract; paragraphs 0030, 033-036, 0057-058). In general the cells are transformed using variety of vectors and constructs and used for functional assay of various analytes including biomolecules such as steroids etc (paragraphs 0096-0099) and in one embodiment the cell plasmids regulates the expression of marker or reporter genes such as luciferase or encoded GFPs (paragraphs 0111-0113) depending on the ligands or their concentrations in the sample. Stuelpnagel et al however, does not teach specific component of a steroid hormone receptor or thyroid hormone receptor.

Quaedackers teaches the limitation of plasmids expressing specific hormone receptors under the control of hormone responsive elements present in 3 random repeats upstream of the minimal adenovirus E1B TATA promoter sequence of SEQ ID NO:2 in pGL3 plasmid and hormone receptors is introduced in the PSG5 expression plasmid in osteoblastic U2-OS cell lines that could be used as an effective cell based detection or assay of several steroid hormones (entire article; abstract;

Thus it would have been obvious for one of ordinary skill in the art to substitute generic biosensor cells in Stuelpnagel live cell based biosensor arrays with Osteoblastic U2-OS cell lines equipped with reporter gene expression under the control of hormone responsive elements present in 3 random repeats upstream of the minimal adenovirus E1B TATA promoter sequence of SEQ ID NO:2 for effectively detecting steroid hormones and related chemical in the cellular environment as taught by Quaedackers and use said cell array for detecting ligands that affect pathways related to steroid receptors. One of ordinary skill in the art would have bee motivated to make and use cell arrays with hormone and related compound detection ability as taught above as they are effective in detecting environmental contaminants of hormonally active ligands/chemicals that could affect human and animal health. One of ordinary skill in the art would have reasonable expectation of success making and using biosensor cell arrays because the art teaches that it is routine to make a biosensor arrays of live cells expressing reporter genes for detecting chemicals affecting any particular cell pathways and the art further teaches that

it is routine to make biosensor cells for detecting specific steroid hormones and related chemicals/ligands in the environment. Thus, the claimed invention was *prima facie* obvious.

Claim 9 is objected-to as it depends from rejected claims. No prior art found on SEQ ID NO:1.

Double Patenting Warning

Applicant is advised that should claim 1 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 4 requires the "array of at least two cell lines", however, such depends from Claim 1, which requires "array of cell lines" implicitly indicating at least two cell lines, therefore, despite a slight difference in wording, Claim 4 is a substantial duplicate of Claim 1.

Applicant is advised that should claim 1 be found allowable, claim 5 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 5 requires "expression plasmids", however, such depends from

Claim 1, which requires "a reporter gene construct", therefore, despite a slight difference in wording, claim 5 is a substantial duplicate of Claim 1.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.,* may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/

Primary Examiner, Art Unit 1633